PB-217 619

INVESTIGATION OF TRITIATED LUMINOUS COMPOUNDS

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31 March 1970

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PB 217 619

1970-13

FINAL REPORT
March 31, 1970

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This project was supported by funds from the Mobility Equipment Research and Development Center, U.S. Army, Fort Belvoir, Virginia.

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INVESTIGATION OF TRITIATED LUMINOUS COMPOUNDS

Radioactive luminous compounds represent a significant potential source of radiation exposure to both industrial workers and the general public. Luminous compounds with tritium as the activating agent are in relatively widespread usage in the painting of watch and instrument dials and in the production of radio-luminescent light sources. It is therefore desirable to have accurate information regarding the degree of uptake and the metabolic behavior of tritiated luminous compounds in general, and comparative data regarding the specific tritiated compounds now in use.

In the present study the GI tract and cutaneous absorptions of four commercially available tritiated luminous compounds ~~was~~ were investigated. The cat was chosen as the experimental animal for studies of GI tract absorption because of the relative similarity of its GI system with that of the human and the fact that it is a convenient experimental animal. Cutaneous absorption of the tritiated compounds was studied in the rat.

Methods

All tritiated luminous compounds now in use and those planned to be used in selected devices were investigated. Four compounds were involved and each was administered to ten test animals in both the cutaneous and GI tract uptake studies with ten control animals given tritiated water. The tritiated compounds evaluated were those produced by:

1. 3M Company (herein abbreviated as MH) specific activity 200 mCi/g or 2.0 mCi per 10 mg dose.

2. Canrad Precision Company (abbreviated as CH) specific activity 250 mCi/g or 2.5 mCi per 10 mg dose.
3. Radium Chemical Company (abbreviated as RH) specific activity 250 mCi/g or 2.5 mCi per 10 mg dose.
4. New England Nuclear Company (abbreviated as NH) specific activity 600 mCi/g or 6.0 mCi per 10 mg dose.

The animals were acclimated for several days in metabolic cages preceeding an experiment. One day prior to the cutaneous exposure of the rats, the animals were weighed and the hair clipped from their backs and shaved. The following day 10 mg of compound was weighed into an area of 1 cm^2 on a piece of plastic foil wrap which was mounted on surgical bandage. The bandage was carefully taped on the rat's back by placing the animal upon the bandage with the compound facing the shaved area. An additional wider piece of surgical tape was placed around the rat's body to hold the compound securely in place.

Eight hours later the bandages were removed, and the remaining compound washed off, ~~being~~ carefully ~~rubbed to~~ spread it over a larger area.

Notes were kept indicating any abrasions or compound remaining on the skin. This was determined with the aid of a flourescent lamp. The rats were returned to proper cages. Urine samples were collected every 12 hours for the first 72 hours and each 24 hours thereafter for periods of from 23 to 30 days. Clean separator funnels were inserted at the beginning of each collection period. Two ml of mineral oil was added to the urine collection vials to prevent evaporation of the sample. The urine sample volumes were noted and an aliquot was counted in a liquid scintillation counter. Results were obtained as nanocuries of tritium per ml of urine.

These same four compounds were fed in 10-mg amounts to cats. A small amount of canned food was fashioned into a cup and the compound was weighed in the cup. The food was then formed into a ball so that the material was in the center. After being without food overnight the cats usually ate the ball of food in one bite. Urine and feces were collected separately every 24 hours. As the activity in the feces was low after 3-4 days, only urine was collected for the remainder of the test period (from 43 to 73 days). These specimens were counted in the same manner as those of the rats.

Curves were plotted of the average daily observed tritium elimination for each experimental group of 10 animals showing urinary tritium activity (nCi/ml) as a function of time. Also plotted were curves of average total daily urinary tritium excretion expressed as a percentage of the administered dose of luminous compound as a function of time.

$$\left(\frac{\text{daily urine activity x urine volume}}{\text{dose of compound}} \times 100\%\right)$$

The percent uptake of tritiated activity was determined by computing the total urinary output of tritium for each animal over the time period followed. This was multiplied by a factor consisting of the total water output (urine, feces, sweat, breath, etc.) for each species divided by the urinary output.[1] This factor was 2.82 for rats and 2.05 for cats. The product so obtained gives the total tritium output via all routes which divided by the dose administered gives the percent absorption.

Urinary elemination data was submitted to least squares regression analysis using a Wang electronic calculator Model 370 produced by Wang

Laboratories, Inc. of Tewksbury, Mass. The effective half-lives for each compound were computed from data so processed. As two components of tritium elemination were observed with each luminous compound after both GI and cutaneous absorption, two half-lives were obtained in each case. The areas under curves representing each of the two individual components were obtained by integration and the ratio of each area to the total area under the excretion curve of the particular compound was computed, giving the percent of total excreted tritium activity due to each component.

A correction factor was derived which when multiplied by the observed total tritium output gives the total tritium excretion which would have been obtained if the urinary output were followed to time equals infinity instead of for a finite number of days. This factor and its duration are given in an appendix.

In order to determine whether the observed two-component elimination of tritium activity was due to the presence of tritium in more than one chemical compound or merely an artifact of absorption, urine from rats administered a tritiated luminous compound (CH) 24 hours previously was divided into two aliquots. The first aliquot was counted for tritium activity immediately (raw) while the second was distilled and the distillate counted. A similar procedure was performed on the urine of rats to whom tritiated water was administered 24 hours previously and luminous compound 8 days previously.

Results

1. Urinary Excretion Curves

Figures 1 and 2 show the observed daily urinary tritium activity

(average of the ten animals in each group) for the different luminous compounds after cutaneous absorption in rats and GI absorption in cats, respectively. These curves all exhibit a two-component elimination, a rapid component being present for the initial 3-4 days post exposure and then yielding to a component with a slower rate of fall. The curve corresponding to the control animals given HTO exhibits only a single-component elimination with a rate of fall similiar to the slow component of the experimental animals.

Formulas obtained by least squares regression analysis corresponding to the daily urinary tritium activity curves in Figures 1 and 2 are shown in Table 1. The curves are seen to represent the sum of two exponential equations. The effective half-lives corresponding to the rapid and the slow components of elimination are shown in Table 2. The slow-component half-lives are seen to be of the same order of magnitude as those of control animals to whom HTO was administered.

Figures 3 and 4 illustrate the total daily urinary excretion expressed as a percent of dose for cutaneous and GI abosrption, respectively. These curves are indicative of the relative absorption of the various luminous compounds.

2. Urine Distillation Experiments

Data showing tritium activity in raw rat urine and in urine distillate for various parameters are shown in Table 3. Activity in the distillate is of necessity due to tritium present in the chemical form of tritiated water (HTO). Raw urine activity is the sum of HTO activity and the activity of any tritium which may be present in other chemical compounds dissolved in the urine. At time 24 hours post exposure to luminous paint

both the rapid and slow half-life components of tritium elimination are present, whereas 8 days after exposure activity due to the fast half-life component is negligible, and essentially all activity is due to the slow component.

At eight days after exposure the ratio of distilled to raw urine activity is seen to approach unity. This is also the case 24 hours after exposure of rats to HTO. This indicates that the slow component of tritium activity is due to tritium absorbed from the luminous compound as HTO. At 24 hours post exposure to luminous compound, however, only 20% of total tritium activity comes over in the distillate. This indicates that the rapid half-life component of tritium activity is due to tritiated compounds other than HTO present as solute in the urine.

3. Tritium Absorption

Table 4 shows the percentage of total tritium activity absorbed through the skin and the GI tract for each luminous compound. The experimentally observed percentage and the percentage corrected for tritium activity which would have been obtained had the experiment been carried to time = infinity are given. There is very little if any significant difference between the observed and corrected values in all cases. The relative absorption among the individual compounds is the same for both routes of absorption in that in each instance the 3M Company compound has the highest degree of absorption followed by Canrad Precision Co., Radium Chemical Co. and New England Nuclear in that order.

Table 5 shows the percentages of the total tritium elimination due to the rapid and slow components, respectively. With the exception of

the 3M company compound, which has the lowest relative percentage of activity due to the fast component after both cutaneous and GI absorption, GI absorption uniformly results in a greater proportion of total tritium activity due to the rapid component.

Discussion

The present study was concerned with the absorption of four tritiated luminous compounds through the gastro-intestinal tract and the skin of experimental animals, and their subsequent metabolism once absorbed.

A study of the daily urinary tritium excretion after administration of all four of these compounds via both routes, revealed a two-component elimination. A rapid component with a half-life of less than one day was invariably found. A slower component was also invariably found, with a half-life of from 3.21 to 4.15 days in rats administered the compounds through the skin and from 7.71 to 9.84 days in cats given the compounds orally. When tritiated water was administered to both experimental animals only one component of urinary elimination was observed within the time period studied with a half-life similar to that of the slower component found in the animals to which the tritiated luminous compounds were administered. This observation suggested that the tritium uptake from the luminous compounds was due in part to the absorption of tritiated water (which is distributed in the total body fluid compartment)which was eliminated as the slow component, and in part to the absorption of other soluble tritiated compounds which probably were distributed in a volume somewhat less than the total body fluid compartment, and were thus being

eliminated at a more rapid rate than tritiated water. An alternative explanation was that the rapid half-life component was an artifact due to some peculiarity of the absorption of the luminous compounds. The former explanation was shown to be correct by studies comparing tritium activity in both raw and distilled urine samples from rats to whom a luminous compound was administered at various time intervals previous to urine collection. At a period of 8 days post exposure, at which time for all purposes only the slower component of tritium is present, approximately 100% of the tritium activity in the urine came over in the distillate, indicating the slow component is due to the elimination of activity absorbed in the form of HTO. Similarly, approximately 100% of the activity came over in the distillate of the urine of rats to whom pure HTO was administered. Twenty-four hours post exposure to a luminous compound, however, at which time both the rapid and slow components are present, only 20% of the total tritium activity came over in the distillate. This would indicate that most of the activity at this time is present in the form of soluble tritiated compounds dissolved in the urine. The exact nature of these compounds has not been determined.

This introduces some difficulties in the calculation of the percent absorption of total tritiated activity from the luminous compounds studied. Most previous work to date has been on the absorption of tritium in the form of tritiated water. As this compound is known to distribute equally within the total body water compartment and all bodily excretions, the percent uptake is calculated by computing the body burden of tritium at some early time post exposure by determining the activity of tritium in

some body fluid such as blood or urine and multiplying this by the body weight of the animal and the percent of the body weight constituted by water. This product divided by the dose administered is taken as the percent absorption.

It cannot be assumed, however, that the rapid component of tritium activity observed in this study distributes equally in the total body water; ~~and~~ hence the application of this method to the calculation of the percent tritium uptake from these luminous compounds would not necessarily be valid. Hence, in this study we determined the total amount of tritium from both components excreted by the animals via the urine. Assuming t'.at both components are also present in the water of other bodily excretions, this value was multiplied by a factor relating water excretion from all routes (urine, breath, feces, etc.) to urine excretion. This product was corrected mathematically to come up with a value which would have been obtained had our observations been carried out for an infinite period of time. The percent absorption thus equaled the total activity eliminated divided by the dose administered.

The data showed a positive correlation between the relative absorption of the various luminous compounds through both the gastrointestinal and cutaneous routes. In both instances the 3M Company compound had the highest rate of absorption, followed in order by the Canrad Precision Company compound, the Radium Chemical Company compound and the New England Nuclear Compound. In addition to having the highest total tritium absorption, the 3M compound had the greatest percentage of the total activity due to the slow component. In the case of an accidental

exposure to a luminous compound, therefore, this particular compound would result in the greatest radiation dose, due to ~~both~~ its greater absolute degree of absorption and the fact that a higher proportion of the activity once absorbed would be eliminated with the slower half-life.

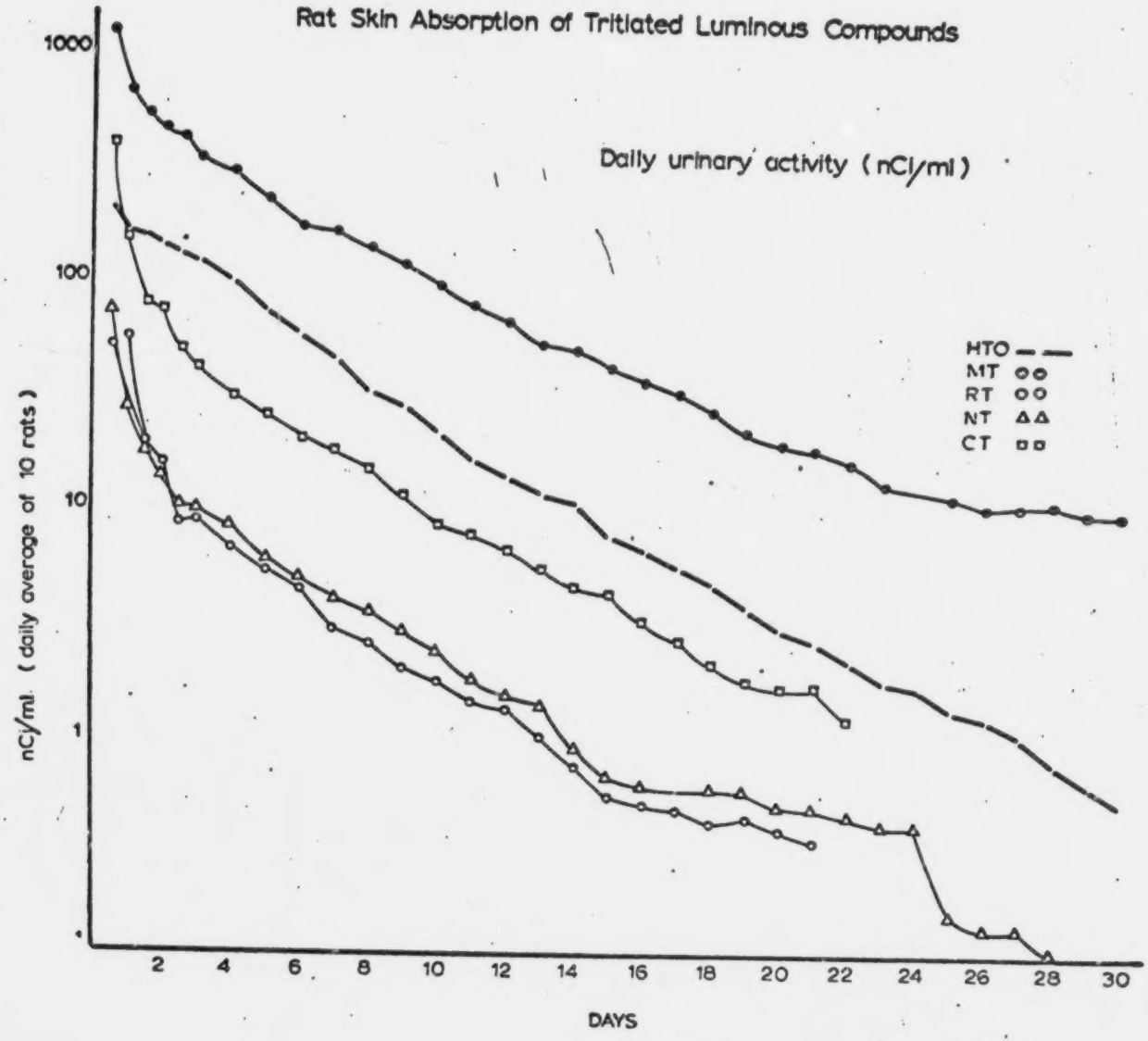
Rat Skin Absorption of Tritiated Luminous Compounds
Daily urinary activity (nCi/ml)
1000
100
10
1
nCi/ml (daily average of 10 rats)
HTO
MT
RT
NT
CT
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
DAYS

Figure 1

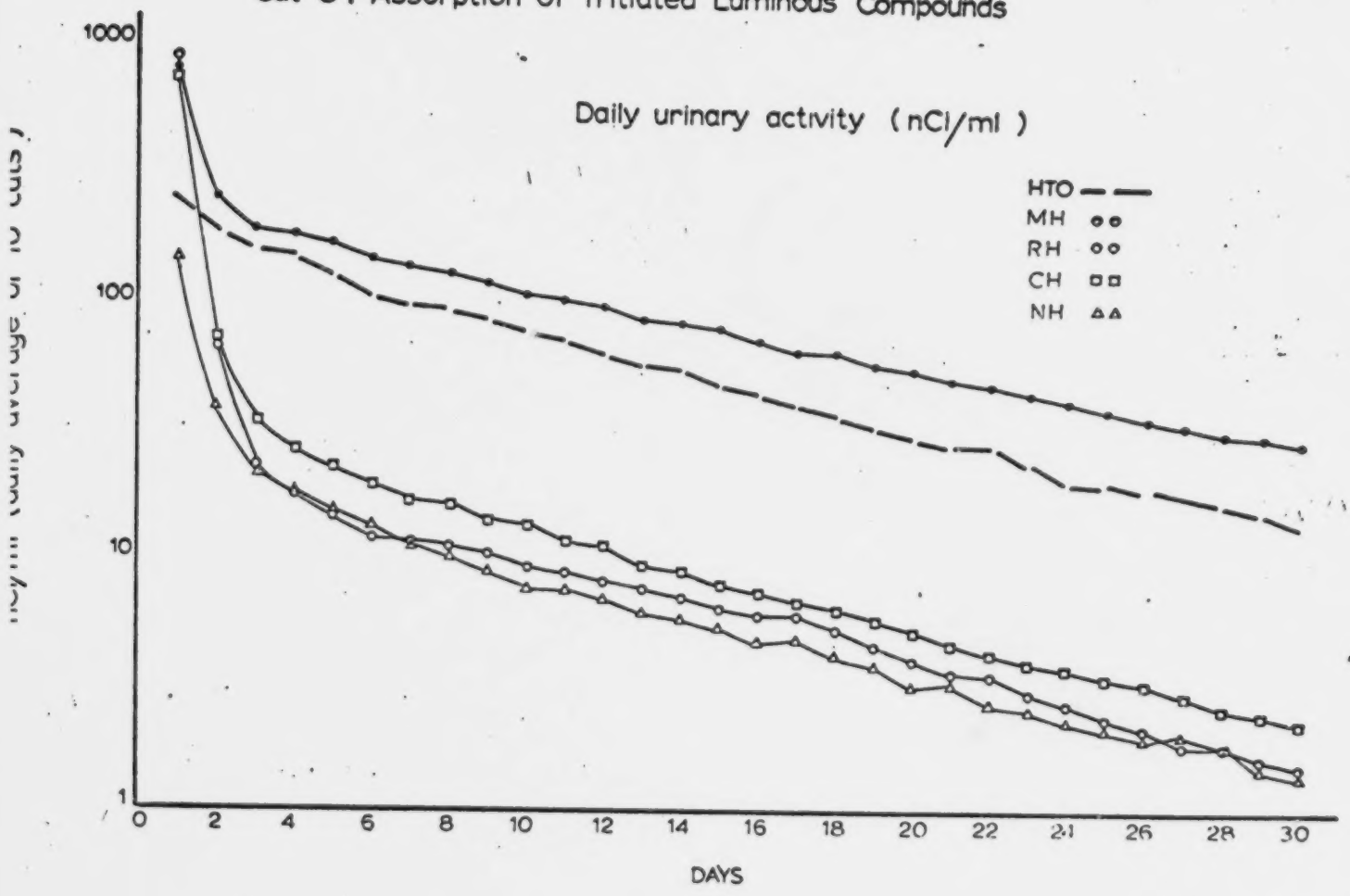
Cat G I Absorption of Tritiated Luminous Compounds
Daily urinary activity (nCi/ml)
HTO
MH
RH
CH
NH
1000
100
10
1
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
DAYS

Figure 2

RAT SKIN ABSORPTION

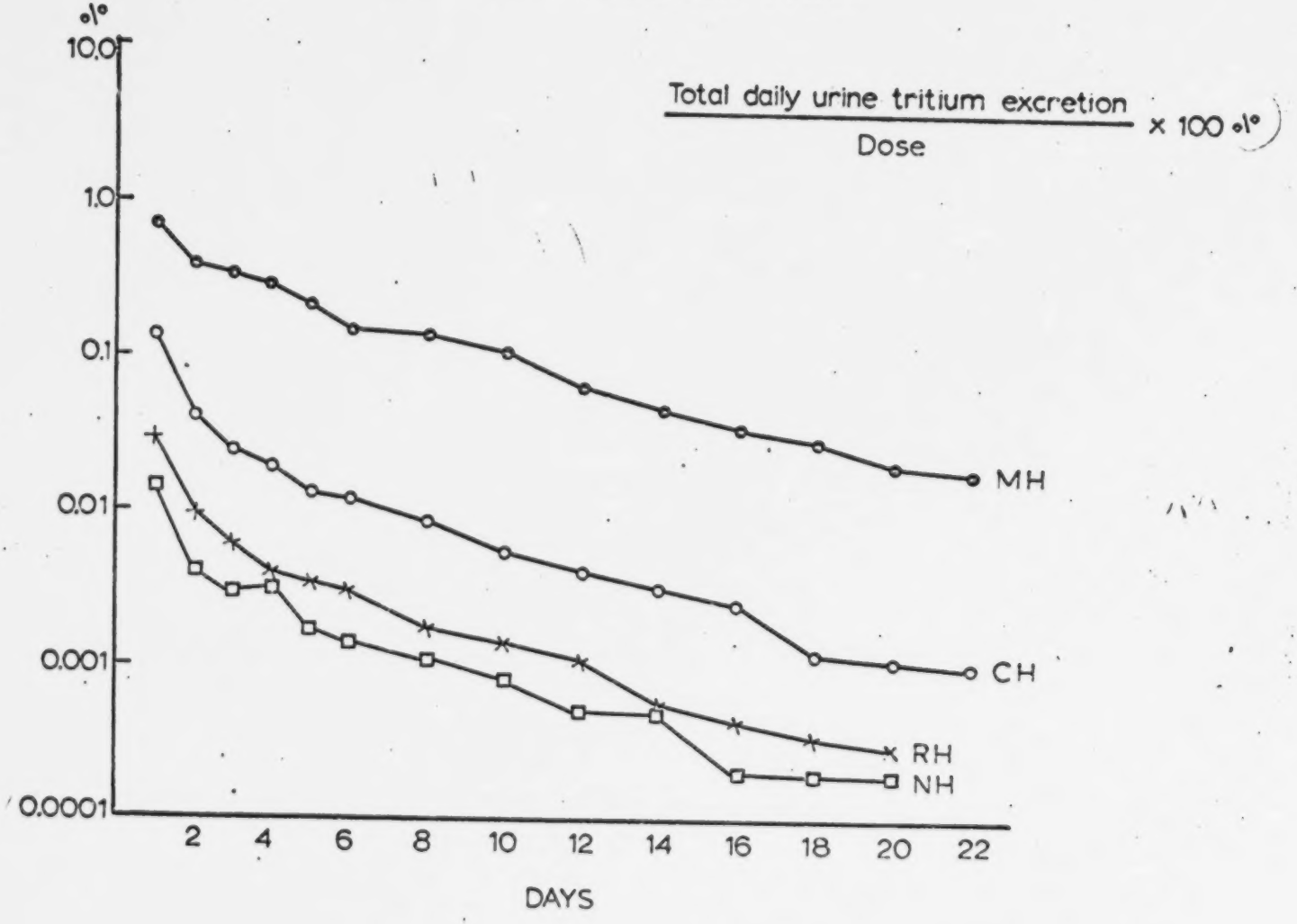

Figure 3

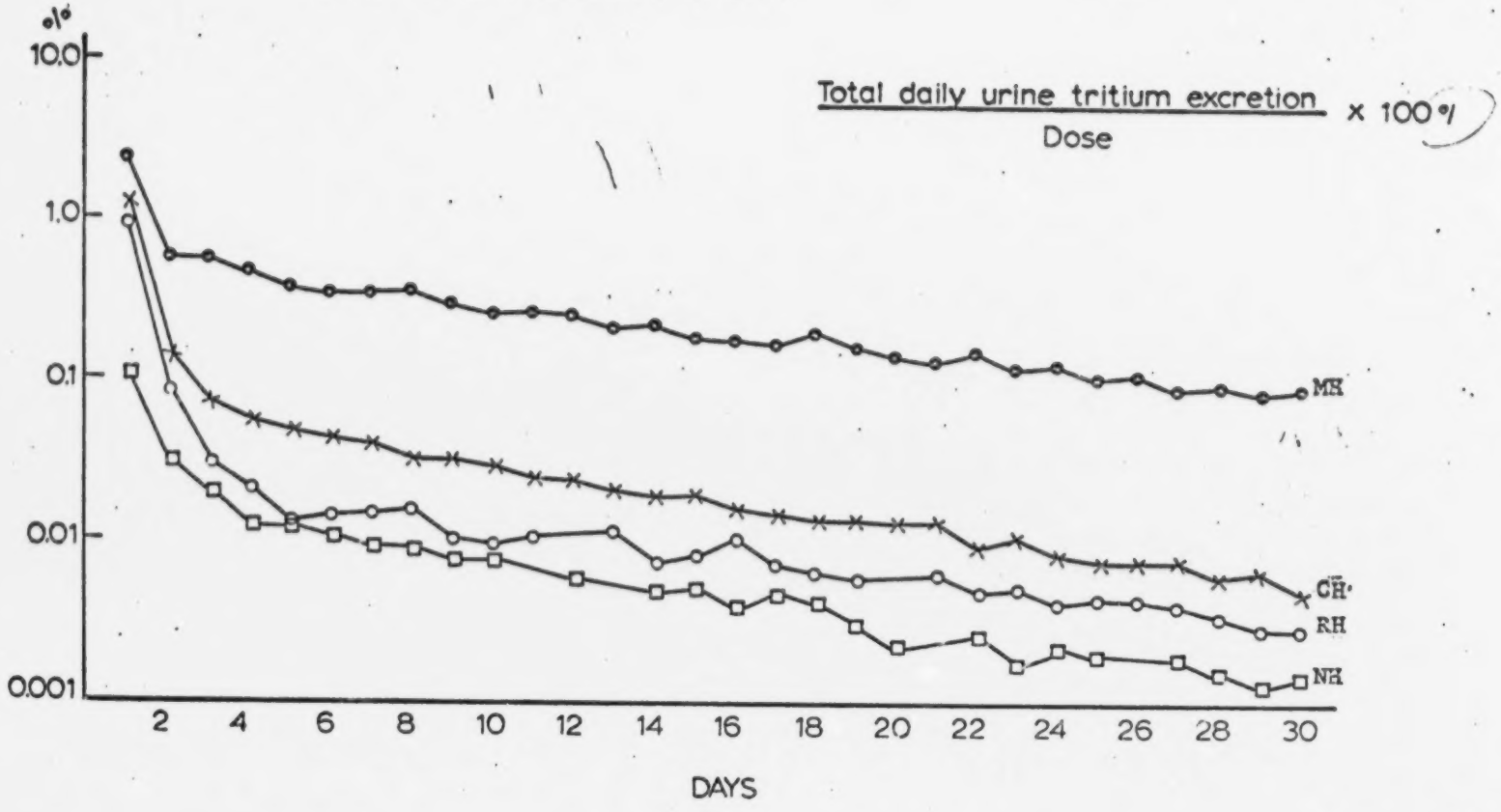
CAT GI ABSORPTION
%
10.0
1.0
0.1
0.01
0.001
Total daily urine tritium excretion / Dose x 100 %
MH
CH
RH
NH
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
DAYS

Figure 4

Table 1

LEAST SQUARES REGRESSION ANALYSIS
FORMULAS OF TRITIUM ELIMINATION CURVES

Cutaneous Absorption in Rats

Compound	
3M Co.	$A = 1130e^{-1.40t} + 450e^{-0.17t}$
Radium Chemical Co.	$A = 89e^{-1.41t} + 14e^{-0.22t}$
New England Nuclear	$A = 142e^{-2.43t} + 18e^{-0.21t}$
Canrad Precision Co.	$A = 304e^{-1.65t} + 54e^{-0.20t}$
HTO (control)	$A = 185e^{-0.22t}$

GI Absorption in Cats

Compound	
3M Co.	$A = 1066e^{-1.14t} + 215e^{-0.07t}$
Radium Chemical Co.	$A = 4020e^{-2.00t} + 20e^{-0.08t}$
New England Nuclear Co.	$A = 305e^{-1.14t} + 18e^{-0.08t}$
Canrad Precision Co.	$A = 2289e^{-1.70t} + 30e^{-0.09t}$
HTO (control)	$A = 191e^{-0.09t}$

A = tritium urinary activity (nCi/ml)

t = time (days)

Table 2

EFFECTIVE HALF-LIVES (DAYS)

Cutaneous Absorption in Rats

Compound	Rapid Component	Slow Component
3M Company	0.50	4.15
Radium Chemical Co.	0.49	3.21
New England Nuclear Co.	0.28	3.21
Canrad Precision Co.	0.42	3.50
HTO(control)	--	3.19

GI Absorption in Cats

Compound	Rapid Component	Slow Component
3M Company	0.61	9.84
Radium Chemical Co.	0.35	8.78
New England Nuclear Co.	0.61	8.25
Canrad Precision Co.	0.41	7.71.
HTO(control)	--	7.44

Table 3

URINE DISTILLATION EXPERIMENTS IN RATS

	Urine Tritium Activity (nCi/ml)		
	Raw	Distilled	Distilled / Raw
Luminous Compound 24 hours post exposure (6)	373.3	73.7	0.20
Luminous Compound 8 days post exposure (5)	66.5	67.7	1.02
HTO - 24 hours post exposure (4)	488.9	564.5	1.15

( ) Number of animals

Table 4

ABSORPTION OF TRITIATED LUMINOUS COMPOUNDS

	Skin Absorption in Rats		GI Absorption in Cats	
Compound	%Absorbed Observed (range) *	%Absorbed Corrected	%Absorbed Observed (range) *	%Absorbed Corrected
New England Nuclear	0.100 (0.063 - 0.274)	0.100	0.66 (0.53 - 0.87)	0.67
Radium Chemical Company	0.189 (0.133 - 0.267	0.199	2.74 (2.11 - 3.26)	2.75
Canrad Precision Company	0.589 (0.318 - 0.925	0.593	4.23 (2.84 - 6.05	4.25
3M Company	8.790 (5.970 - 11.000)	8.830	21.44 (18.23- 24.58)	21.55

* Average of 10 animals

Table 5

PERCENT TOTAL TRITIUM ELIMINATION DUE TO VARIOUS COMPONENTS
(time 0 to infinity)

	Skin Absorption in Rats		GIAbsorption in Cats	
Compound	Rapid Component	Slow Component	Rapid Component	Slow Component
New England Nuclear	41.3	58.7	55.1	44.9
Radium Chemical Company	43.1	56.9	88.6	11.4
Canrad Precision Company	40.3	59.7	79.9	20.1
3M Company	23.1	76.9	23.5	76.5

Appendix

Correction Factor - derivation

$$\text{Observed total excreted activity (time 0 to t)} = ff\left[\text{true total excreted activity (time 0 to infinity)}\right] + sf\left[\text{true total excreted activity (time 0 to infinity)}\right]\left[\frac{\text{Area (0 to t)}}{\text{Area (0 to infinity)}}\right]$$

Where ff = fraction total tritium output due to fast component (table 5)

sf = fraction of total tritium output due to slow component (table 5)

$sf + ff = 1$

t = time urine output followed (days)

Area = integrated area under slow component urine excretion curve.

It is assumed that for the fast component 100% of all activity is excreted within the time period followed (minimum of approximately 47 half-lives in these experiments.

$$\text{true total excreted activity (time 0 to infinity)} = \frac{\text{Observed total excreted activity (time 0 to t)}}{ff + sf\left[\frac{\text{Area (0 to t)}}{\text{Area (0 to infinity)}}\right]}$$

Reference

1. Spector, William S., editor Handbook of Biological Data, National Academy of Sciences, National Research Council, p. 339, W. B. Saunders Co. Philadephia 1956.